

REMARKS

A. Status of Claims

Claims 1-16 are pending prior to the entry of the present amendment. Of the preceding claims, 1-4 and 6-10 are currently amended. Claim 5 is canceled and claims 12-16 are withdrawn from consideration.

Specifically, claim 1 is amended to delete recitations of non-elected species and to correct certain inadvertent typographical errors. Additionally, the limitations of canceled claim 5 are incorporated into claim 1 and the term "hydrate" is deleted from this claim. No new matter is introduced by the instant amendments and, accordingly, entry thereof is respectfully requested.

Claims 2-4 and 6-10 are amended to delete the term "hydrate" and to correct certain inadvertent typographical errors. No new matter is introduced by the instant amendments and, accordingly, entry thereof is respectfully requested.

After the entry of the present Amendment, Claims 1-4 and 6-11 are pending.

B. Claim Rejections – 35 U.S.C. §112, First Paragraph

Claims 1-11 - The Examiner indicates that the specification, while being enabling for pharmaceutically acceptable salts, allegedly does not reasonably provide enablement for a hydrate. Specifically, the Examiner states:

Claims 1-11 are rejected under 35 U.S.C 112, first paragraph, because the specification, while being enabling for pharmaceutically acceptable salts of formula (I), does not reasonably provide enablement for a hydrate. ...

(Office Action mailed March 30, 2009, page 3)

Applicants acknowledge the Examiner's indication that the pharmaceutically acceptable salts are fully enabled by the specification. To expedite prosecution, and without prejudice, claims 1-4 and 6-10 are amended to delete the term "hydrate". Said amendment is without prejudice, and Applicants do not acknowledge the propriety of the enablement rejection, and the Examiner's justification thereof.

In light of the instant amendments, Applicants respectfully request withdrawal of the 35 U.S.C. §112 rejection and allowance of Claims 1-4 and 6-11.

C. Claim Rejections – 35 U.S.C. §112, Second Paragraph

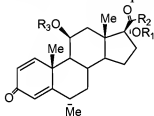
Claim 8 - The Examiner has rejected claim 8 as being indefinite for lacking a period.

A period has been added at the end of claim 8. Applicants respectfully request withdrawal of the 35 U.S.C. §112 rejection and allowance of Claim 8.

D. Claim Rejections – 35 U.S.C. §103

Claims 1-4, 6, 7 and 11 - The Examiner has rejected Claims 1-4, 6, 7 and 11 under 35 U.S.C. §103(a) as allegedly being unpatentable over Roberts et al. (WO98/20151; hereinafter, "Roberts"). In particular, the Examiner states:

Roberts teaches the production of adrenocorticoid steroids of the formula:



...
The instant claims differ from the reference by reciting the corresponding 17-carbamoyloxy derivative of the exemplified prior art compound. However, the reference teaches an equivalent between acyl and carbamoyl groups in the 17-position (see definition of R₁ and R₃ on page 4, lines 1-2). ...

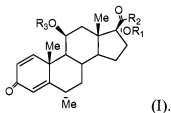
(Office Action mailed March 30, 2009, page 7) Applicants respectfully traverse this rejection as the Examiner has not made out a prima facie case of obviousness over Roberts.

Court has consistently held that a § 103(a) rejection as related to a new chemical compound must provide some suggestion or motivation combined with a reasonable expectation of success. The Federal Circuit reasoned in *Takeda* that "a case of *prima facie* obviousness with respect to chemical compounds requires a showing that the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention." 492 F.3d 1350

(Fed. Cir. 2007). The court made it clear that "consistent with the legal principles enunciated in *KSR*," there must be "some reason that would have led a chemist to modify a known compound in a particular manner."

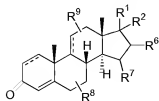
Eisai affirmed *Takeda* and further elaborated on the 103 obviousness analysis as related to new chemical compounds. *Eisai v. Dr. Reddy's*, 533 F.3d 1353 (Fed. Cir. 2008). The court stated that "[t]o the extent an art is unpredictable, as the chemical arts often are, *KSR*'s focus on these "identified, predictable solutions" may present a difficult hurdle because potential solutions are less likely to be genuinely predictable". *Id* at 1359. The court further stated that "post-*KSR*, a prima facie case of obviousness for a chemical compound still, in general, begins with reasoned identification of a lead compound. *Teva* cannot create a genuine issue of material fact on obviousness through the unsupported assertion that compounds other than landsoprazole might have served as lead compounds". *Id*.

Instant claim 1 and its dependent claims 2-4, 6, 7 and 11 are not obvious over Roberts as the compounds of the instant claims (hereinafter, "Instant Compounds") have very different chemical structures from the compounds disclosed in Roberts (hereinafter, "Roberts Compounds"). In particular, Roberts Compounds have the following structure:



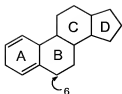
(Roberts, claim 1, page 23)

On the other hand, Instant Compounds of claim 1 have the following structure:



, wherein R^2 is $-O-C(O)-N(R^3)(R^4)$, ... R^8 is halo ...

For ease of discussion, the following designations of rings and positions, which may or may not be the same as those used in Roberts or the instant application, are used in the



following discussion:

It can be seen from the above structures there are at least two differences between Roberts Compounds and Instant Compounds. First, Roberts Compounds are substituted by a methyl group at the 6 position of the B ring. In contrast, there is no methyl substitution at any position on the B ring of the Instant Compounds. Second, the B ring of Roberts Compounds has no halo substitution. On the other hand, the B ring of Instant Compounds is substituted by a halo.

Roberts also does not provide any suggestion or motivation for identifying the right lead compounds and making the specific modifications necessary to arrive at Instant Compounds. It would take at least two steps from Roberts Compounds to arrive at Instant Compounds. First, a skilled artisan would have to identify Roberts Compounds wherein R_1 is carbamoyl as the lead compounds for further modification. Second, the skilled artisan would have to modify the lead compounds by removing the methyl group from the 6 position of the B ring and, additionally, add a halo substitution to this ring of the lead compounds. Roberts simply fails to provide any suggestion or motivation to do either as discussed in more detail below.

A skilled artisan would not pick Roberts Compounds wherein R_1 is carbamoyl as the lead compounds since this reference provides no such suggestion or motivation. Roberts discloses, generically, that R_1 may be carbamoyl among several possible choices: " R_1 may be H, alkyl, substituted alkyl, silyl, acyl, acyloxy or carbamoyl". (Roberts, lines 1-2, page 4) This reference, however, does not in any way suggest that R_1 being carbamoyl provides any advantages. In fact, other than the generic structure, no specific example with R_1 being carbamoyl is disclosed in this reference.

Moreover, even assuming *arguendo* that Roberts would suggest the right lead compounds, which it does not, this reference also fails to provide any suggestion or motivation to make the specific modifications necessary to arrive at Instant Compounds. To arrive at Instant Compounds from Roberts Compounds, a skilled artisan would have to remove the methyl group from the 6 position of the B ring and add a halo group to this same ring. Among all adrenocorticoid steroid compounds disclosed in Roberts, every compound has a methyl

substitution at the 6 position on the B ring. There is no teaching or suggestion in Roberts that this methyl group should be removed or modified. Thus, a skilled artisan would understand that the presence of this group at this position is important and would not be motivated to remove this group from the lead compounds.

Furthermore, no adrenocorticoid steroid compound disclosed in Roberts has a halo substitution on the B ring and there is no teaching or suggestion in this reference that a halo group should be added to the B ring to obtain desirable compound. In light of this lack of teaching or suggestion, a skilled artisan would not be motivated to make this modification.

Therefore, instant Claims 1-4, 6, 7 and 11 are not obvious over Roberts as this reference fails to provide any reason or suggestion to select the right lead compounds and then modify these compounds in the particular way to arrive at the Instant Compounds.

E. Summary

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration of the pending claims and reexamination of the application. Timely allowance of the pending claims is respectfully requested.

If a telephonic communication with the Applicant's representative will advance the prosecution of the instant application, please telephone the representative indicated below. Applicants believe no additional fees are due, but the Commissioner is authorized to charge any fees required in connection with this response to Merck Deposit Account No. 13-2755.

Respectfully submitted,

By /Yong Zhao, Reg. # 57014/
Yong Zhao
Reg. No. 57,014
Attorney for Applicants

MERCK & CO., INC.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-7338

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